

REMARKS

Review and reconsideration on the merits are requested.

New claims are added. Basis for the new claims is later explained.

A telephone interview was conducted concerning this application. The independent claims were discussed, and all of the prior art was discussed, namely, Kennedy, Jichlinski, Kajiware and Jaffe.

With respect to the individual teachings of the references, during the interview these were discussed as presented herein.

The main point made during the interview, however, was that the prior art lacked any teaching of going from *in vivo* fluorescence testing to NMR testing, i.e., the essential argument was that if fluorescence testing works well (Jichlinski), where is the motivation on this record to label using the carbon or nitrogen isotope and also use NMR?

The Examiner's basic position was that one of ordinary skill in the art would find it obvious that labeled 5-ALA must be used with NMR, and it is well known that NMR would give higher sensitivity.

However, Applicants adhere to their position that on this record there was nothing to support the Examiner's position.

It is believed that the prior art can reasonably be characterized as follows, and this was basically the characterization presented during the interview.

Kajiware (based on the translation) reasonably teaches a method for producing carbon-13-labeled 5-ALA and derivatives thereof. Kajiware does not deal with treatment of living

animals in any substantial fashion. The utility disclosed in Kajiwara is that the PBG produced is useful, e.g., as a therapeutic drug for lead poisoning.

Kennedy teaches that 5-ALA can be administered to patients with certain types of cancer and this leads to a preferential accumulation of fluorescing and/or photosensitizing concentrations of Proto IX within the malignant cells. Subsequent exposure of such cancers to photoactivating light may cause selective destruction of the malignant tissue by photodynamic action, with sparing of adjacent normal tissues. ALA-induced fluorescence and statistically significant photosensitization is disclosed.

Jaffe is more or less a technical treatise which shows that ^{13}C -NMR can be used to observe non-protonated carbons or deuterated carbons as ligands bound to PBGS.

Jichlinski discloses fluorescence photodetection of neoplastic urothelial foci in bladder cancer following intravesical installation of 5-ALA. Jichlinski also discloses that fluorescence imaging is extremely helpful in finding and treating any residual disease at the end of the transurethral bladder resection. However, Jichlinski also teaches that the prognostic value of the dysplastic changes revealed on bladder mucosa still remains to be elucidated.

From the above discussion of the individual teachings of the prior art, the basis for Applicants argument regarding a lack of motivation to go from *in vivo* fluorescence to NMR testing using labeled 5-ALA is believed clear.

With respect to the newly added claims, Applicants believe that there is no teaching in the prior art that the malignant tumor can be detected with higher sensitivity using NMR as compared to the case where 5-ALA per se is used.

Applicants believe that there is no suggestion in the prior art of detection using a plurality of NMR.

Given the silence of the prior art upon using labeled 5-ALA in combination with NMR, clearly there is no suggestion of using the dosages claimed.

Finally, Applicants believe that there is no suggestion that when diagnosis and treatment are simultaneously carried out, the economical burden can be reduced by decreasing the isotope purity through the addition of isotope-free 5-ALA.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.


Basis for the added claims is as follows:

<u>Claim(s)</u>	<u>Basis</u>
14, 15	Page 4, lines 1-3
16, 17	Page 4, last line - page 5, line 5
18-25	Page 5, lines 6-11 and line 22; page 6, line 4
26, 27	Page 6, lines 11-14
28-37	Species of independent claims

AMENDMENT UNDER 37 C.F.R. § 1.111
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38, 39	Page 16, lines 3-6 from the bottom of the page
40, 41	Simply to emphasize the same 5-ALA isotope is used
42, 43	Page 27, line 9
44, 45	Page 17 lines 12-16
46	Same as claim 13.

Respectfully submitted,


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